

REMARKS

This application is a divisional of US 09/806,437, now issued as US 6,756,483. Claims 1-7 were pending in the application at the time of filing. In response to a restriction requirement dated July 5, 2006, Applicants elected Group VI (claims 1-5, 7) drawn to a method for the differential-diagnostic early detection and detection of a pro-atrial-natriuretic peptide (proANP or pro-ANF). Claims 1- 7 are cancelled above and new claims 8-10 are presented. Claims 8-10, therefore, are pending in the application.

Claims 1-7 are cancelled above and rewritten as new claims 8-10. No new matter is presented by the amendment.

Rejection Under 35 U.S.C. §112, first paragraph

Claims 1-5 and 7 are rejected under 35 U.S.C. §112, first paragraph as failing to comply with the written description and enablement requirements.

New claim 8 above is directed to a method for the detection of sepsis in an individual suspected of having sepsis, the method comprising obtaining a plasma or serum sample from the individual, contacting said sample with an antibody specific for pro-atrial natriuretic factor (pro-ANF) and determining the level of pro-ANF, wherein an increased level of pro-ANF as compared to healthy individuals is indicative of sepsis. Support for new claims 8 is found in the specification at page 18, line 24 to page 19, line 3 and in Figure 6.

Applicant urges that the specification contains an adequate description marker of interest (of a method for detecting/diagnosing sepsis by determining the level of pro-ANF in a biological fluid from a patient in whom sepsis is suspected by using an antibody that is specific for pro-ANF, the precursor to atrial natriuretic factor (ANF) and that one of skill would be able to practice the claimed invention without undue experimentation.

Accordingly, withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Rejection Under 35 U.S.C. §102

Original claims 1-5 and 7 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Lubbesmeyer et al. because Lubbesmeyer et al. teaches detection of sepsis in sheep by an immunoassay of plasma in which ANF is detected.

The present claims are directed to a method for the detection of sepsis in a patient by determining the level of *pro*-ANF in a sample from the patient. Lubbesmeyer et al. teaches that ANF was isolated from rat atrial muscle and identified as having diuretic and natriuretic activity (page R570, column 1, 2nd full paragraph with reference (11) to DeBold et al. 1981.) The teachings of Lubbesmeyer et al., therefore, are directed to the detection of the mature peptide hormone, ANF.

Subsequently, DeBold's lab published the amino acid sequence of the 28 amino acid peptide hormone (Flynn et al., *The amino acid sequence of an atrial peptide with potent diuretic and natriuretic properties*. Biochem biophys res Commun. 117(3): 859-65 1983; the abstract is submitted herewith for the examiner's convenience.)

The present invention on the other hand measures the level of a precursor to ANF, *pro*-ANF, a molecule that is larger than the mature peptide hormone. The amino acid sequence of ANF as disclosed by Flynn et al. corresponds to the 28 amino acid sequence of the carboxy terminus of the ANF precursor (roughly amino acids 100 to 128).

The present specification teaches that the Prepro-ANF 26-55 (human) RIA kit from DRG Instruments GmbH was used to detect the levels of *pro*-ANF in the sera of sepsis patients. The antibodies in this kit were generated to amino acids 26-55 (amino terminus) of the precursor sequence.

Thus, while Lubbesmeyer et al. discloses the presence of the mature ANF peptide hormone, it does not teach or fairly suggest the presence of the pro-hormone, pro-ANF in sepsis patients and therefore, cannot anticipate Applicants claimed invention.

Withdrawal of the rejection under 35 U.S.C. §102(b) is respectfully requested.

It is respectfully submitted that the above-identified application is now in a condition for allowance and favorable reconsideration and prompt allowance of these claims are respectfully requested. Should the Examiner believe that anything further is desirable in order to place the application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,



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